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CULTURING INTRAVASCULAR CATHETER SEGMENTS

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FOREWORD

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Principal Investigator's Signature 20 May 92
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INTRODUCTION

Semiquantitative culture of catheter segments, as originally described by Maki¹, is widely used in identification of infections associated with intravascular catheters. It is considered the easiest and most labor efficient method available to detect catheter associated infection.² It has been used in studies looking at rates of infection in different types of catheters,³⁻⁵ risk factors for the development of catheter-related complications,⁶ and methods of identifying catheter-related infection.⁷⁻¹² In all of these, the catheter tip was transported to the lab for culture.

Based on observed discrepancies between Gram stain and semiquantitative culture results, two of these studies suggested the possibility that routine transport and handling of catheter tips, prior to culturing, leads to loss of viable organisms.^{7,10} Because of it's important role in identifying catheter-related infections and because of the concerns raised by these authors, we attempted to prospectively evaluate the hypothesis that routine laboratory culture of catheter tips is associated with decreased sensitivity compared to cultures plated at the bedside.

METHODS AND MATERIALS

CATHETER COLLECTION

Intravascular catheters located in central veins of adult surgical and medical intensive care patients were cultured. Any type of central venous catheter was accepted for study.

In our intensive care units, catheter sites are covered with clear or opaque occlusive dressings, which are changed at either 72 hours or 24 hours, respectively. Antibiotic ointment is not routinely used. Any central catheters placed outside the ICU setting (except in the operating room) are considered contaminated and replaced. Multiple guidewire exchanges are allowed and are mandatory at 5 day intervals. Multiple exchanges of Swan-Ganz pulmonary artery catheters are allowed. Otherwise, absolute indications for catheter exchange or removal are the same as those suggested by Norwood¹³.

Prior to working in the intensive care units, all housestaff were required to be familiar with procedures for removal of catheters, exchange of catheters over guidewire using the Seldinger technique, bedside plating of catheter segments and preparation of segments for transport to the microbiology lab. This was accomplished by requiring housestaff to view a training film produced specifically for this protocol.

Catheters were removed by the physician(s) responsible for the patient's care, using strict aseptic technique. Sterile

gowns and gloves, sterile barriers and caps were required. The skin surrounding the insertion point was cleaned with povidone-iodine and allowed to dry. Removal was accomplished using sterile scissors and forceps.

The last 6 cm. of each catheter was divided into two 3 cm. subsegments; a distal segment (including the tip) and one just proximal to that. The 6 cm. total segment length was chosen because this closely approximates Maki's original catheter length¹, and is the length used in other studies.^{5,8,10} Catheter tip cultures were chosen over intracutaneous segment cultures because the intracutaneous segment is more difficult to culture² and does not appear to provide significantly different results from the distal tip^{2,12}. The catheter tip is also widely used.^{3,4,5,6,7,8,9,10,11,14}

For the first approximately 100 catheters, the proximal subsegment was plated onto agar immediately at the bedside and the distal portion was transported to the lab for culture in the usual manner. For the next approximately 100 catheters, the distal subsegment was plated at the bedside and the proximal portion sent to the lab. There were cases where subsegments were cultured in reverse of that prescribed by protocol. These cases were included in the final analysis, with the appropriate location of culture being noted.

At the time of catheter removal, physicians were asked to fill out a data form. Information on the form included: type of catheter, site of removal, reason for removal and if other sites

of infection were suspected or documented. Blood cultures were obtained when bacteremia was suspected and were not a requirement of this protocol.

Catheters from patients less than 18 years of age, cases where culture data was not available for both catheter subsegments and any contaminated catheter tips (growth of ≥ 3 different organisms on semiquantitative culture plate) were excluded from the study.

This study was approved by the institutional committee on human research.

CATHETER CULTURES

Catheter subsegments sent to the lab were cultured using semiquantitative technique described by Maki.¹ The catheter subsegments were plated onto 5% sheep-blood agar and incubated at 37 degrees centigrade. Inspection of the plates for microbial growth was done daily and colony counts were performed by visual inspection. Isolate identification was accomplished by standard microbiologic methods.

For catheter subsegments cultured immediately at the bedside, the segment was transferred to a plate containing 5% sheep-blood agar using sterile forceps. It was then rolled over the surface 4 to 5 times, while avoiding plating the same area more than once. These plates were then incubated at 37 degrees centigrade, in a portable incubator located in the intensive care

unit until they were transported to the microbiology lab. Transport was accomplished within 24-48 hours. Subsequent processing was identical to that of subsegments cultured in the lab as described above.

DEFINITIONS

Catheter-related infection is defined as microbial growth of ≥ 15 colonies per semiquantitative agar plate.¹³ Catheter-related bacteremia (includes fungemia) is defined as isolation of the same organism from catheter segment and at least one blood culture drawn from a different site within 48 hours of catheter removal, in the absence of other suspected or documented sources of infection. The catheter was considered to be hematogenously seeded if there were other suspected or documented foci of infection.

Full concordance between catheter subsegments is defined as growth of ≥ 15 colonies of only the same organism(s) on both subsegments. Partial concordance between catheter subsegments is defined as growth of ≥ 15 colonies of at least one of the same organisms on both catheter segments.

STATISTICAL METHODS

Using the STATISTIX 3.1 software package, paired comparison of semiquantitative cultures was accomplished using the McNemar test for symmetry. Sensitivity, specificity, positive and negative predictive values were calculated using standard statistical methods.

RESULTS

One-hundred ninety-seven catheters from 92 patients were analyzed. The patient population included 63 males and 29 females with a mean age of 63.7 years (range 20 to 92 years). All catheters were central venous catheters, including 76 triple lumen catheters, 60 Swan-Ganz pulmonary artery catheters, 54 Cordis introducer catheters, 5 single lumen catheters and 1 dialysis catheter (SEE TABLE 1). The type of catheter was not specified in one case. Ninety-two catheters were from the internal jugular vein, 49 from the subclavian vein, 34 from the femoral vein and 4 from other sites (mostly external jugular). In 18 cases, the site of insertion was not reported.

Semiquantitative cultures of 31 (15.7%) catheter tips were positive for ≥ 15 colonies per plate (SEE TABLE 2). Nine of these grew more than one organism. Plating onto agar at the bedside resulted in 28 of 197 cases (14.2%) growing ≥ 15 colonies per plate. Laboratory plating of specimens submitted in sterile tubes resulted in 13 of 197 cases (6.6%) growing ≥ 15 colonies per plate. Ten of these cases were positive both at the bedside and in the lab. Cultures were exclusively positive in 3 catheters plated in the lab, whereas positive cultures were found exclusively in 18 catheters plated immediately at the bedside. This discrepancy was statistically significant ($p=.0011$; McNemar's test for symmetry). The sensitivity and specificity of sending catheters to the lab for culture, assuming bedside

plating as the "gold standard", would be 36% and 98%, respectively.

During the first half of the study, when the proximal subsegment was plated at the bedside and the distal subsegment was plated in the lab, the difference between exclusively positive cultures at the bedside (12) versus exclusively positive cultures in the lab (2) was associated with a p value of 0.008 (n=93). During the second half of the study, when the distal subsegment was plated at the bedside and the proximal subsegment in the lab, the difference between exclusively positive cultures at the bedside (6) versus exclusively positive cultures in the lab (1) was associated with a p value of 0.059 (n=104).

Fifty-four organisms showed significant growth on semiquantitative culture (SEE TABLE 3). For purposes of tabulation, each organism from multiply colonized catheters was designated separately. Coagulase negative staphylococcus was the most commonly isolated organism (25 of 54 organisms). In cases where only bedside plating revealed ≥ 15 colonies, the most commonly cultured organism was also coagulase negative staphylococcus (10 of 21 organisms). Bedside plated cultures identified infection with yeast (2), pseudomonas aeruginosa (2), staphylococcus aureus (1), staphylococcus heamolyticus (2) and others (4), when laboratory plated cultures were negative. In the 10 cases where laboratory plating and bedside plating were both positive, there was total concordance among organisms in 8 cases and partial concordance in the rest.

Seven organisms caused catheter-related bacteremia in 5 cases. Two of these cases occurred in the group of catheters positive only at the bedside. One of the catheters positive only in the lab resulted in catheter-related bacteremia.

Contamination of either bedside plated agar (21), laboratory plated agar (4), or both (4), resulted in exclusion from analysis of 29 cases of paired data. The majority of bedside plated agar contamination occurred early in the study.

DISCUSSION

A semiquantitative catheter tip culture yielding growth of ≥ 15 colonies of bacteria on blood agar serves as a useful marker for the development of subsequent catheter-related bacteremia and sepsis. This association is true for both predominantly peripheral catheters¹ and predominantly central venous catheters.^{7,8,12} For this reason, a positive culture is considered an indication for removal of the catheter from the insertion site.¹³ Anything which interferes with the growth of significant numbers of colonies on blood agar results in loss of the opportunity to identify catheters at risk for bacteremia. Our study is the first to evaluate whether the current practice of sending catheter tips to the lab results in a lower sensitivity for catheter-related infection, compared to bedside culturing.

In 1985, Cooper and others⁷ reported on the use of Gram stain to rapidly identify catheter-associated infection. In this study of 330 catheters from 224 patients they found 9 cases where a positive Gram stain was associated with growth of < 15 colonies on blood agar. Most of these organisms were yeast, and 4 of these catheters were associated with fungemia. The authors stated that "at least some of the catheters that we have designated as having false positive Gram stains may instead have had false negative cultures.....It is conceivable that organisms,

such as candida, that thrive in moist environments may not survive for a prolonged period on dry plastic surfaces. It is perhaps relevant that most catheters in this study were held for one to two hours or longer before cultures were performed." In 1987 Collignon and others¹⁰ also compared Gram stained "impression smears" of intravascular catheters to semiquantitative cultures of 322 catheters. In 16 cases Gram stain showed $\geq 2+$ organisms when colony count was < 15 colonies. The authors stated that "The reasons these catheters were negative on semiquantitative culture are unclear.....the possibility (exists) that transport in a "dry" container may have resulted in loss of viability." The results of our study, demonstrating a significantly higher yield of positive catheter tips at the bedside, including two fungal cultures positive only at the bedside, adds to this literature and supports the premise that the delay associated with routine laboratory culture of catheter tips results in loss of viable organisms.

In this study, the rate of catheter-related infection in cultures plated at the bedside was higher (14.2%) than in those cultures plated in the lab (6.6%). In the literature, the rate of catheter-related infection has been reported to be anywhere from 10-14%¹⁴, although direct comparisons between multiple studies are not easy to make. This is primarily due to the large number of factors influencing microbial colonization of intravascular catheters which cannot be controlled for, ^{13,15} as well as the different definitions and terms used to identify

infection. However, in the two studies where specimens were reportedly taken to the lab immediately and immediately plated,^{3,9} the rate of catheter-related infection was higher than that reported in the remaining literature. Together, these observations add support to the hypothesis that routine laboratory culture of catheter tips is associated with a lower yield, compared to immediate culture.

Bedside plating of catheter tip cultures has previously been used to study infection associated with arterial catheters.¹⁶ Its successful use requires that blood-sheep agar plates must be available in the intensive care unit and that physicians handling the specimens must be familiar with culture plating techniques. Also, an incubator may be required if these plates are not taken to the lab immediately. Considering the benefits of increased detection of catheter-related infection, these requirements appear reasonable to us.

Two findings require additional comment. First, the rate of contamination in bedside cultured agar (21), compared to the rate of contamination of laboratory plated specimens (4), was high. This was felt to be due to presence of a learning curve associated with bedside plating of cultures and is supported by the fact that the majority of these contaminations occurred early in the study. Second, the difference between exclusively positive bedside-plated cultures and exclusively positive laboratory-plated cultures during the second half of the study was associated with a p value of 0.059. We attributed this to

the smaller number of infected catheter subsegments during this time period. When the results from both proximal and distal subsegments were combined (representative of the entire 6 cm. segment usually cultured), there was a statistically higher incidence of bedside-positive catheter cultures.

CONCLUSIONS

Culture of catheter tips at the bedside provides significantly more positive results than cultures plated in the laboratory. Identifying more catheter-related infections may further decrease the incidence of catheter-related bacteremia and sepsis. When attempting to diagnose a catheter-related infection, bedside plating of catheter tip cultures should be considered in place of sending catheters to laboratory for routine culture.

REFERENCES

- 1 . Maki DG, Weise CE, Sarafin HW. A semiquantitative method for identifying intravenous-catheter-related infection.
NEJM 1977;296:1305-1309.
2. Collignon PJ, Munro R. Laboratory diagnosis of catheter associated sepsis. Eur J Clin Microbiol Infect Dis
1989;8:807-814.
3. Gil RT, Kruse JA, Thill-Baharozian MC, Carlson RW.
Triple-vs. Single-Lumen Central Venous Catheters: A
prospective study in a critically ill population.
Arch Intern Med 1989;149:1139-1143.
4. Yeung C, May J, Hughes R. Infection rates for single lumen
v. triple lumen subclavian catheters.
Infect Control Hosp Epidemiol 1988;9:154-158.
5. Hilton E, Haslett TM, Borenstein MT, Tucci V,
Isenberg HD, Singer C. Central catheter infections:
single-versus triple-lumen catheters: Influence of guidewire
on infection rates when used for replacement of catheters.
AJM 1988;84:667-672.

REFERENCES

6. Richet H, Hubert B, Nitemberg G, Andreumont A, Buu-Hoi A, Ourbak P, et al. Prospective multicenter study of vascular catheter-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. J Clin Microbiol 1990;28:2520-2525.
7. Cooper GL, Hopkins CC. Rapid diagnosis of intravascular catheter-associated infection by direct gram staining of catheter segments. NEJM 1985;312:1142-1147.
8. Collignon PJ, Soni N, Pearson IV, Woods P, Munro R, Sorrell TC. Is semiquantitative culture of central vein catheter tips useful in the diagnosis of catheter-associated bacteremia? J Clin Microbiol 1986;24:532-535.
9. Cercenado E, Ena J, Rodriguez-Creixems M, Romero I, Bouza E. A conservative procedure for the diagnosis of catheter-related infections. Arch Intern Med 1990;150:1417-1420.
10. Collignon P, Chan R, Munro R. Rapid diagnosis of intravascular catheter-related sepsis. Arch Intern Med 1987;147:1609-1612.

REFERENCES

11. Coutlee F, Lemieux C, Paradis JF. Value of direct catheter staining in the diagnosis of intravascular-catheter-related infection. J Clin Microbiol 1988;26:1088-1090.
12. Moyer MA, Edwards LD, Farley L. Comparative culture methods on 101 intravenous catheters; Routine, semiquantitative, and blood cultures. Arch Intern Med 1983;143:66-69.
13. Norwood S, Ruby A, Civetta J, Cortes V. Catheter-related infections and associated septicemia. Chest 1991;99:968-975.
14. Snyder RH, Archer FJ, Endy T, Allen TW, Condon B, Kaiser J. Catheter infection: A comparison of two catheter maintenance techniques. Annals of Surgery 1988;208:651-653.
15. Elliott TSJ. Intravascular-device infections. J Med Microbiol 1988;27:161-167.
16. Norwood SH, Cormier B, McMahon NG, Moss A, Moore, V. Prospective study of catheter-related infection during prolonged arterial catheterization. Crit Care Med 1988;16:836-839.

APPENDIX

TABLE 1. CATHETER DEMOGRAPHICS

TYPE OF CATHETER

| | | |
|-------------------|----|-------|
| triple lumen | 76 | (39%) |
| Swan-Ganz | 60 | (30%) |
| Cordis introducer | 54 | (27%) |
| single lumen | 5 | (3%) |
| dialysis | 1 | (.5%) |
| not specified | 1 | (.5%) |

SITE OF INSERTION

| | | |
|------------------|----|-------|
| internal jugular | 92 | (47%) |
| subclavian | 49 | (25%) |
| femoral | 34 | (17%) |
| other | 4 | (2%) |
| not reported | 18 | (9%) |

TABLE 2. FREQUENCY OF DISTRIBUTION OF SEMIQUANTITATIVE CULTURES

| | | <u>AGAR</u> (bedside plating) | |
|------------------------------|--|-------------------------------|--|
| | | <u>< 15 colonies</u> | <u>≥ 15 colonies</u> (one or more organisms) |
| <u>TUBE</u> (lab plating) | <u>< 15 colonies</u> | 166 | 18 |
| | <u>≥ 15 colonies</u> (one or more organisms) | 3 | 10 |

TABLE 3. ORGANISMS YIELDING GROWTH ON SEMIQUANTITATIVE PLATE

| | <u>TOTAL</u> | <u>POSITIVE</u> | <u>POSITIVE</u> |
|------------------------------|-----------------|-----------------|-----------------|
| | <u>POSITIVE</u> | <u>BEDSIDE</u> | <u>LAB</u> |
| | | <u>ONLY</u> | <u>ONLY</u> |
| Coagulase Negative | | | |
| Staphylococcus | 25 | 10 | 3 |
| Yeast (3 C. albicans; 1 | | | |
| not identified) | 4 | 2 | - |
| Serratia marcescens | 4 | - | - |
| Citrobacter freundii | 4 | - | - |
| Staphylococcus aureus | 3 | 1 | - |
| Enterococcus | 3 | - | - |
| Pseudomonas aeruginosa | 2 | 2 | - |
| Staphylococcus haemolyticus | 2 | 2 | - |
| Other: (Bacillus spp.(1), | 7 | 4 | - |
| Enterobacter Cloacae(1), | | | |
| Beta-strep(2), Staph spp.(3) | | | |
| (not further identified)) | | | |